and a resurfaced antibody or antigen-binding fragment thereof.

D8

32. (Thrice Amended) The method of claim 30, wherein the antibody binds to an epitope included in amino acid residues of about 87-108 (SEQ ID NO:1) or about 59-80 (SEQ ID NO:2) of hTNFα.

D9

34. (Twice Amended) The method of claim 30, wherein the antibody is a chimeric antibody, said chimeric antibody comprising (a) a non-human variable region specific for TNF or an antigen-binding portion thereof and (b) a human constant region.

D10

35. (Thrice Amended) The method of claim 34, wherein the chimeric antibody binds to an epitope included in amino acid residues of about 87-108 (SEQ ID NO:1) or about 59-80 (SEQ ID NO:2) of hTNFα.

D11

36. (Twice Amended) The method of claim 34, wherein the chimeric antibody competitively inhibits binding of TNFα to monoclonal antibody cA2.

37. (Twice Amended) The method of claim 36, wherein the chimeric antibody is monoclonal antibody cA2.

REMARKS

Claims 6, 8-10, 12-15, 29-32 and 34-37 are pending and under examination in the subject application. Applicants have amended the claims in order to introduce certain format changes.

Applicants maintain that these amendments raise no issue of new matter, and respectfully request entry of this Preliminary Amendment. Upon entry of this Preliminary Amendment, claims 6, 8-10, 12-15, 29-32 and 34-37 will still be pending and under examination.

Pursuant to the requirements of 37 C.F.R. 1.121(b)(2), applicants annex hereto as Exhibit A claims 6, 8-10, 12-15, 29-32 and 34-37 marked up to show the changes made herein relative to the previous version of those claims.

In view of the arguments set forth below, applicants maintain that the Examiner's objections and rejections made in the September 13, 2000 Office Action have been overcome, and respectfully request that the Examiner reconsider and withdraw same.

The Claimed Invention

This invention provides methods of treating or preventing thrombosis, and decreasing plasma fibrinogen. These methods comprise administering a tumor necrosis factor antagonist to a subject *diagnosed as suffering from or at risk of thrombosis*.

This invention is based on applicants' *surprising discovery* that inhibiting the biological activity of TNFα reduces fibrinogen levels in subjects suffering from or at risk of thrombosis. Since fibrinogen plays an integral role in forming thrombi, this invention has considerable use for treating and preventing

thrombosis in subjects diagnosed as suffering from or at risk thereof.

Rejection Under 35 U.S.C. §102(b)

The Examiner rejected claims 6, 8-10, 12-15, 29-32 and 34-37 under 35 U.S.C. §102(b) as allegedly anticipated by WO 92/16553 ("'553 Application") as "evidenced" by Wolfe, et al. (Arthritis and Rheumatism, 1994, Vol. 4, No. 4, pp. 481-491).

In response to the Examiner's rejection, applicants respectfully traverse.

Briefly, claims 6, 8-10, 12-15, 29-32 and 34-37 provide a method of treating or preventing thrombosis in a subject *diagnosed as* suffering from or at risk thereof. The method comprises administering to the subject a therapeutically effective amount of a TNF antagonist.

To anticipate the claimed method, the '553 Application would have to teach each and every element thereof. It fails to do this.

Instead, the '553 Application teaches the use of anti-TNFα antibodies to treat TNFα-mediated pathologies generally. It does not list thrombosis among such pathologies. In fact, nowhere does it even *mention* the term "thrombosis", let alone teach methods of treating or preventing it. The '553 Application also fails to teach the use of TNF antagonists to decrease plasma fibrinogen in

an individual diagnosed as suffering from or at risk of thrombosis.

Wolfe, et al. do nothing to cure this shortcoming. This reference merely describes different causes of death and accompanying mortality rates for rheumatoid arthritis patients. Thrombosis is not included in the disorders described by Wolfe, et al.

Applicants further point out that even if the incidence of thrombosis among rheumatoid arthritis patients were taught by the '553 Application, which it is not, this reference still would not anticipate the rejected claims. That is, this reference also fails to teach the element of a subject *already* diagnosed as suffering from thrombosis or at risk thereof. The mere *possibility* of thrombosis occurring in rheumatoid arthritis patients cannot substitute for this element.

For these reasons, the '553 Application, as "evidenced" by Wolfe, et al., fails to teach each and every element of the rejected claims.

In view of the above remarks, applicants maintain that claims 6, 8-10, 12-15, 29-32 and 34-37 satisfy the requirements of 35 U.S.C. §102(b).

Rejection Under 35 U.S.C. §102(e)

The Examiner rejected claims 6, 8-10, 12-15, 29-32 and 34-37 under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent No.

5,598,195 ("'195 Patent") as "evidenced" by Wolfe, et al.

In response to the Examiner's rejection, applicants respectfully traverse, and maintain that the '195 Patent fails to teach each and every element of the rejected claims.

The rejected claims and the Wolfe, et al. reference are discussed above.

The '195 Patent teaches methods of treating TNF-mediated pathologies, specifically rheumatoid arthritis, using anti-TNF antibodies. It does *not* list thrombosis among the pathologies treated. In fact, like the '553 Application, the '195 Patent fails to teach methods of treating or preventing thrombosis, fails to teach subjects already diagnosed as suffering from thrombosis or at risk thereof, and fails even to mention the term "thrombosis." Also, like the '553 Application, the '195 Patent fails to teach using TNF antagonists to decrease plasma fibrinogen in subjects diagnosed as suffering from or at risk of thrombosis. For the reasons stated above with respect to the '553 Application, Wolfe, et al. do not cure these deficiencies.

Therefore, the '195 Patent, as "evidenced" by Wolfe, et al., fails to teach each and every element of the rejected claims.

In view of the above remarks, applicants maintain that claims 6, 8-10, 12-15, 29-32 and 34-37 satisfy the requirements of 35 U.S.C. §102(e).

Summary

In view of the amendments and remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the enclosed $1600.00, which includes the $710.00 CPA filing fee and the $890.00 fee for an additional three-month extension of time, is deemed necessary in connection with the filing of this Preliminary Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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